AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 1, line 6 with the following rewritten paragraph:

--This application claims priority under 35 U.S.C. Section 119(e) to U.S. Provisional Application Serial No. ~~60,217,671~~ 60/217,617, entitled Instrumentation and Methods for Electrical Stimulation filed on July 10, 2000, which application is hereby incorporated by reference in its entirety. This application is also related to the following three additional U.S. Patent Applications, which were filed simultaneously with the present application; all of these are also incorporated by reference to this application in their entireties:

Application Serial No. 09/804,457, entitled ION CHANNEL ASSAY METHODS, filed March 12, 2001 ~~attorney docket AUROBIO.026A~~;

Application Serial No. 09/804,480, entitled ION CHANNEL ASSAY METHODS, filed March 12, 2001 ~~attorney docket AUROBIO.026DV1~~ ; and

Application Serial No. 09/804,580, entitled HIGH THROUGHPUT METHOD AND SYSTEM FOR SCREENING CANDIDATE COMPOUNDS FOR ACTIVITY AGAINST TARGET ION CHANNELS, filed March 12, 2001, now U.S. Pat. No. 6,686,193 ~~, attorney docket AUROBIO.026DV2~~.

Please replace the paragraph beginning at page 51, line 29 with the following rewritten paragraph:

--In some cases it may be preferred to add, or load one, or more of the FRET reagents with one or more light absorbing substances in order to reduce undesired light emission, as for example described in commonly owned U.S. patent application Ser. No. 09/118,497, filed Jul.

17, 1998, now U.S. Pat. No. 6,200,762; U.S. patent application Ser. No. 09/120,516, filed Jul. 21, 1998, now U.S. Pat. No. 6,214,563; and U.S. patent application Ser. No. 09/122,477 filed Jul. 23, 1998, now U.S. Pat. No. 6,221,612. --

Please replace the paragraph beginning at page 52, line 3 with the following rewritten paragraph:

--FRET based voltage sensors may also be derived from the use of other membrane targeted fluorophores in conjunction with a mobile hydrophobic donor or acceptor. Other such compositions are disclosed, for example, in U.S. patent application Ser. No. 09/459,956, filed Dec. 13, 1999, now U.S. Pat. No. 6,342,379. --

Please replace the paragraph beginning at page 52, line 7 with the following rewritten paragraph:

--Suitable instrumentation for measuring transmembrane potential changes via optical methods includes microscopes, multiwell plate readers and other instrumentation that is capable of rapid, sensitive ratiometric fluorescence detection. A preferred instrument of this type is described in U.S. patent application Ser. No. 09/118,728 filed Jul. 17, 1998, now U.S. Pat. No. 6,608,671. This instrument (the Voltage/Ion Probe Reader or VIPR™) is an integrated liquid handler and kinetic fluorescence reader for 96-well and greater multiwell plates. The VIPR™ reader integrates an eight channel liquid handler, a multiwell positioning stage and a fiber-optic illumination and detection system. The system is designed to measure fluorescence from a column of eight wells simultaneously before, during and after the introduction of liquid sample obtained from another microtiter plate or trough. The VIPR™ reader excites and detects emission signals from the bottom of a multiwell plate by employing eight trifurcated optical bundles (one bundle for each well). One leg of the trifurcated fiber is used as an excitation source, the other two legs of the trifurcated fiber being used to detect fluorescence emission. A ball lens on the end

of the fiber increases the efficiency of light excitation and collection. The bifurcated emission fibers allow the reader to detect two emission signals simultaneously and are compatible with rapid signals generated by the FRET-based voltage dyes. Photomultiplier tubes then detect emission fluorescence, enabling sub-second emission ratio detection. --

Please replace the paragraph beginning at page 86, line 25 with the following rewritten paragraph:

--Additional toxicological analysis of candidate modulators can be established by determining in vitro toxicity towards a cell line, such as a mammalian (preferably human) cell line. Candidate modulators can be treated with, for example, tissue extracts, such as preparations of liver, such as microsomal preparations, to determine increased or decreased toxicological properties of the chemical after being metabolized by a whole organism, or via their ability to be degraded via Cytochrome P450 systems as described in commonly owned U.S. patent application Ser. No. 09/301,525, filed Apr. 28, 1999, now U.S. Pat. No. 6,420,130; U.S. patent application Ser. No. 09/301,395 filed Apr. 28, 1999, now U.S. Pat. No. 6,143,492; and U.S. application Ser. No. 09/458,927 filed Dec. 10, 1999, now U.S. Pat. No. 6,514,687. The results of these types of studies are often predictive of toxicological properties of chemicals in animals, such as mammals, including humans. --

Please replace the paragraph beginning at page 87, line 5 with the following rewritten paragraph:

--The toxicological activity can be measured using reporter genes that are activated during toxicological activity or by cell lysis (see WO 98/13353, published Apr. 2, 1998). Preferred reporter genes produce a fluorescent or luminescent translational product (such as, for example, a Green Fluorescent Protein (see, for example, U.S. Pat. No. 5,625,048 to Tsien et al., issued Apr. 29, 1998; U.S. Pat. No. 5,777,079 to Tsien et al., issued Jul. 7, 1998; WO 96/23810

to Tsien, published Aug. 8, 1996; WO 97/28261, published Aug. 7, 1997; PCT/US97/12410, filed Jul. 16, 1997, now published as WO 98/02571; PCT/US97/14593~~595~~, filed Aug. 15, 1997, now published as WO 98/06737) or a translational product that can produce a fluorescent or luminescent product (such as, for example, beta-lactamase (see, for example, U.S. Pat. No. 5,741,657 to Tsien, issued Apr. 21, 1998, and WO 96/30540, published Oct. 3, 1996)), such as an enzymatic degradation product. Cell lysis can be detected in the present invention as a reduction in a fluorescence signal from at least one photon-producing agent within a cell in the presence of at least one photon reducing agent. Such toxicological determinations can be made using prokaryotic or eukaryotic cells, optionally using toxicological profiling, such as described in PCT/US94/00583, filed Jan. 21, 1994 (WO 94/17208), German Patent No 69406772.5-08, issued Nov. 25, 1997; EPC 0680517, issued Nov. 12, 1994; U.S. Pat. No. 5,589,337, issued Dec. 31, 1996; EPO 651825, issued Jan. 14, 1998; and U.S. Pat. No. 5,585,232, issued Dec. 17, 1996).

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